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**TRANSMITTAL  
FORM**

(to be used for all correspondence after initial filing)

|                               |                        |
|-------------------------------|------------------------|
| <b>Application Number</b>     | 09/310,844             |
| <b>Filing Date</b>            | May 12, 1999           |
| <b>First Named Inventor</b>   | David J. Ecker         |
| <b>Group Art Unit</b>         | 1635                   |
| <b>Examiner Name</b>          | M. Schmidt             |
| <b>Attorney Docket Number</b> | IBIS0058-100/IBIS-0171 |

Total Number of Pages in This Submission

**ENCLOSURES (check all that apply)**

|   |  |   |         |  |
|---|--|---|---------|--|
| <input type="checkbox"/> Fee Transmittal Form<br><input type="checkbox"/> Fee Attached<br><input type="checkbox"/> Amendment / Response<br><input type="checkbox"/> After Final<br><input type="checkbox"/> Affidavits/declaration(s)<br><input type="checkbox"/> Extension of Time Request<br><input type="checkbox"/> Express Abandonment Request<br><input type="checkbox"/> Information Disclosure Statement<br><input type="checkbox"/> Certified Copy of Priority Document(s)<br><input type="checkbox"/> Response to Missing Parts/ Incomplete Application<br><input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53 | <input type="checkbox"/> Assignment Papers (for an Application)<br><input type="checkbox"/> Drawing(s)<br><input type="checkbox"/> Licensing-related Papers<br><input type="checkbox"/> Petition<br><input type="checkbox"/> Petition to Convert to a Provisional Application<br><input checked="" type="checkbox"/> Power of Attorney with Revocation and Change of Correspondence Address<br><input type="checkbox"/> Terminal Disclaimer<br><input type="checkbox"/> Request for Refund<br><input type="checkbox"/> CD, Number of CD(s) | <input type="checkbox"/> After Allowance Communication to Group<br><input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences<br><input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief)<br><input type="checkbox"/> Proprietary Information<br><input type="checkbox"/> Status Letter<br><input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):<br>Table A<br>Statement Under 37 CFR 3.73(b) with executed Assignment |         |  |
| <table border="1"> <tr> <td>Remarks</td> <td></td> </tr> </table>   |  |   | Remarks |  |
| Remarks   |  |   |         |  |

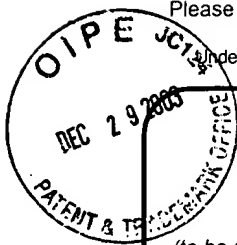
**SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT**

|                         |  |
|-------------------------|--|
| Firm or Individual name | Paul K. Legaard, Registration No. 38,534 |
| Signature               | <i>Paul K. Legaard</i>                   |
| Date                    | 23 DECEMBER 2003                         |

**CERTIFICATE OF MAILING**

|   |  |      |                  |
|---|--|------|------------------|
| I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on this date: 23 DECEMBER 2003 |  |      |                  |
| Typed or printed name   | Paul K. Legaard, Registration No. 38,534 |      |                  |
| Signature   | <i>Paul K. Legaard</i>                   | Date | 23 DECEMBER 2003 |

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.





**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

**STATEMENT UNDER 37 CFR 3.73(b)**

Applicant, **ISIS Pharmaceuticals, Inc., a corporation**, states that it is:

☒ the assignee of the entire right, title, and interest of the patent applications identified in Table A attached hereto.

The extent (by, percentage) of its ownership interest is **100%** in the patent applications identified in Table A.

☒ a copy of the pertinent assignment from the inventor(s) of the patent applications identified in Table A is enclosed herewith.

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

Respectfully submitted,  
**ISIS PHARMACEUTICALS, INC.**

Date: 11-6-03

By: \_\_\_\_\_

Name: B. Lynne Parshall  
Title: Executive Vice President

DOCKET NO.: IBIS-0171

PATENT

## A S S I G N M E N T

WHEREAS, We, David J. Ecker of Encinitas, California, Richard Griffey of Vista, California, Stanley T. Crooke of Carlsbad, California, Ranga Sampath of San Diego, California, Eric Swayze of Carlsbad, California, Venkatraman Mohan of Carlsbad, California, Steven Hofstadler of Oceanside, California, John McNeil of La Jolla, California, have invented a certain invention entitled **MOLECULAR INTERACTION SITES OF INTERLEUKIN-2 RNA AND METHODS OF MODULATING THE SAME**, for which we have made application for Letters Patent of the United States, said application having been filed on **May 12, 1999 and assigned Application No. 09/310,844**; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal

representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

Dated: 6/30, 1999David J. Ecker  
(David J. Ecker)State of California           )  
  )  
County of San Diego        )       ss.

On this 30th day of June, 1999, before me, the undersigned, a Notary Public for the state, personally appeared (**David J. Ecker**) personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

Carol A. Collins  
Signature of Notary

Dated: JUNE 29, 1999Richard Griffey  
(Richard Griffey)

State of California            )  
  )       ss.  
County of San Diego         )

On this 29<sup>th</sup> day of June, 1999, before me, the undersigned, a Notary Public for the state, personally appeared (**Richard Griffey**) personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

Carol A. Collins  
Signature of Notary

DOCKET NO.: IBIS-0171

PATENT

Dated: 6/30, 1999

(Stanley T. Crooke)

State of California )  
 ) ss.  
County of San Diego )


On this 30<sup>th</sup> day of June, 1999, before me, the undersigned, a Notary Public for the state, personally appeared (Stanley T. Crooke) personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



Carol A. Collins  
Signature of Notary

Dated: 7/7, 1999


  
(Ranga Sampath)

State of California                    )  
  )       ss.  
County of San Diego                 )

On this 7<sup>th</sup> day of July, 1999, before me, the undersigned, a Notary Public for the state, personally appeared **(Ranga Sampath)** personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

  
Signature of Notary



**DOCKET NO.: IBIS-0171**

# PATENT

Dated: 6/29/99, 1999

Eric Swayze  
(Eric Swayze)

State of California                    )  
  )        ss.  
County of San Diego                 )

On this 29<sup>th</sup> day of JUNE, 1999, before me, the undersigned, a Notary Public for the state, personally appeared (**Eric Swayze**) personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

**WITNESS my hand and official seal.**



Carol A. Collins  
Signature of Notary

DOCKET NO.: IBIS-0171

PATENT

Dated: 6/30, 1999

Venkatraman Mohan  
(Venkatraman Mohan)

State of California            )  
  )    ss.  
County of San Diego         )

On this 30<sup>th</sup> day of June, 1999, before me, the undersigned, a Notary Public for the state, personally appeared (Venkatraman Mohan) personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



Carol A. Collins  
Signature of Notary

DOCKET NO.: IBIS-0171

PATENT

Dated: 6/30, 1999

Steven Hofstadler  
(Steven Hofstadler)

State of California           )  
  )  
County of San Diego        )       ss.

On this 30<sup>th</sup> day of June, 1999, before me, the undersigned, a Notary Public for the state, personally appeared (Steven Hofstadler) personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

Carol A. Collins  
Signature of Notary

DOCKET NO.: IBIS-0171

PATENT

Dated: 6/29/99, 1999

  
(John McNeil)

State of California       )  
                                  )  
County of San Diego       )       ss.

On this 29<sup>th</sup> day of JUNE, 1999, before me, the undersigned, a Notary Public for the state, personally appeared (**John McNeil**) personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



Carol A. Collins  
Signature of Notary

Table A

| Serial No.<br>Patent No.<br>Docket No.  | Filing Date<br>Issue Date               | Inventor(s)            | Examiner       | Art Unit | Title   |
|---|---|------------------------|----------------|----------|---|
| 09/200,355<br>6,451,524<br>IBIS0010-100 | November 25, 1998<br>September 17, 2002 | David J. Ecker         | J. Fredman     | 1655     | Identification of Disease<br>Predictive Nucleic Acids   |
| 09/200,107<br>6,492,111<br>IBIS0034-100 | November 25, 1998<br>December 10, 1998  | David J. Ecker         | J. Fredman     | 1634     | <i>IN SITU</i> Binary Synthesis of<br>Biologically Effective<br>Molecules                                 |
| 10/209,761<br>IBIS0034-101              | August 1, 2003                          | David J. Ecker         | To Be Assigned | 1634     | <i>IN SITU</i> Binary Synthesis of<br>Biologically Effective<br>Molecules                                 |
| 09/076,440<br>6,221,587<br>IBIS0035-100 | May 12, 1998<br>April 24, 2001          | David J. Ecker et al.  | E. Campbell    | 1656     | Identification of Molecular<br>Interaction Sites in RNA for<br>Novel Drug Discovery                       |
| 09/310,667<br>IBIS0035-101              | May 12, 1999                            | David J. Ecker et al.  | F. Lu          | 1634     | Identification of Molecular<br>Interaction Sites in RNA for<br>Novel Drug Discovery                       |
| 09/076,405<br>IBIS0036-100              | May 12, 1998                            | Richard Griffey et al. | S. Broda       | 2123     | Generation of Virtual<br>Combinatorial Libraries of<br>Compounds  |
| 09/753,869<br>IBIS0036-101              | January 3, 2001                         | Richard Griffey et al. | M. Borin       | 1631     | Generation of Virtual<br>Combinatorial Libraries of<br>Compounds  |
| 09/076,447<br>IBIS0037-100              | May 12, 1998                            | Richard Griffey et al. | J. Fredman     | 1655     | Characterization of<br>Interactions Between<br>Molecular Interaction Sites of<br>RNA and Ligands Therefor |



|   |                                    |                           |                  |                |  |
|---|------------------------------------|---------------------------|------------------|----------------|--|
| 09/310,653<br>IBIS0037-101              | May 12, 1999                       | Richard Griffey et al.    | J. Fredman       | 1637           | Characterization of Interactions Between Molecular Interaction Sites of RNA and Ligands Therefor   |
| 09/076,206<br>6,428,956<br>IBIS0038-100 | May 12, 1998<br>August 6, 2001     | Stanley T. Crooke et al.  | S. Ztiomer       | 1634           | Mass Spectrometric Methods for Biomolecular Screening  |
| 09/260,310<br>6,329,146<br>IBIS0038-101 | March 2, 1999<br>December 11, 2001 | Stanley T. Crooke         | S. Ztiomer       | 1634           | Mass Spectrometric Methods for Biomolecular Screening  |
| 09/884,317<br>IBIS0038-102              | June 19, 2001                      | Stanley T. Crooke         | A. Chakrabarti   | 1634           | Mass Spectrometric Methods for Biomolecular Screening  |
| 09/884,317<br>IBIS0038-103              | June 27, 2003                      | Stanley T. Crooke         | To Be Determined |                | Mass Spectrometric Methods for Biomolecular Screening  |
| 09/076,214<br>IBIS0039-100              | May 12, 1998                       | Richard H. Griffey et al. | T. Friend        | 1639           | Generation of Combinatorial Libraries of Compounds Corresponding to Virtual Libraries of Compounds |
| 09/400,150<br>IBIS0039-101              | September 21, 1999                 | Richard H. Griffey et al. | M. Tran          | 1639           | Generation of Combinatorial Libraries of Compounds Corresponding to Virtual Libraries of Compounds |
| 60/085,092<br>IBIS0040-001              | May 12, 1998                       | Stanley T. Crooke         | Not applicable   | Not applicable | Small Molecule Targeting Of RNA Structures   |
| 09/076,404<br>IBIS0040-100              | May 12, 1998                       | David J. Ecker et al.     | A. Marschel      | 1631           | Identification of Molecular Interaction Sites in RNA for Novel Drug Discovery                      |
| 09/310,735<br>IBIS0040-101              | May 12, 1999                       | David J. Ecker et al.     | A. Marschel      | 1631           | Modulation of Molecular Interaction Sites on RNA and Other Biomolecules                            |



|                            |                 |                       |                |                |   |
|----------------------------|-----------------|-----------------------|----------------|----------------|---|
| 10/104,949<br>IBIS0040-102 | March 22, 2002  | David J. Ecker et al. | A. Marschel    | 1631           | Modulation of Molecular Interaction Sites on RNA and Other Biomolecules                       |
| 09/310,907<br>IBIS0041-100 | May 12, 1999    | David J. Ecker et al. | A. Marschel    | 1631           | Molecular Interaction Sites of Vimentin RNA and Methods of Modulating the Same                |
| 10/135,017<br>IBIS0041-101 | April 24, 2002  | David J. Ecker et al. | A. Marschel    | 1631           | Molecular Interaction Sites of Vimentin RNA and Methods of Modulating the Same                |
| 09/310,761<br>IBIS0042-100 | May 12, 1999    | David J. Ecker et al. | M. Schmidt     | 1635           | Molecular Interaction Sites of Ornithine Decarboxylase RNA and Methods of Modulating the Same |
| 60/314,236<br>IBIS0043-001 | August 22, 2001 | David J. Ecker        | Not Applicable | Not Applicable | Molecular Interaction Sites of Hepatitis C Virus RNA and Methods of Modulating the Same       |
| 10/225,501<br>IBIS0043-100 | August 19, 2002 | David J. Ecker        | To Be Assigned | 1645           | Methods for Identifying Ligand Binding Sites in a Biomolecule                                 |
| 60/314,251<br>IBIS0044-001 | August 22, 2001 | David J. Ecker        | Not Applicable | Not Applicable | Molecular Interaction Sites of 23S Ribosomal RNA and Methods of Modulating the Same           |
| 10/224,836<br>IBIS0044-100 | August 20, 2002 | David J. Ecker        | To Be Assigned | 1645           | Molecular Interaction Sites in 23S Ribosomal RNA and Methods of Modulating the Same           |
| 60/314,020<br>IBIS0045-001 | August 21, 2001 | David J. Ecker        | Not Applicable | Not Applicable | Molecular Interaction Sites of RNase P RNA and Methods of Modulating the Same                 |



|                            |                   |                           |                |                |   |
|----------------------------|-------------------|---------------------------|----------------|----------------|---|
| 10/223,156<br>IBIS0045-100 | August 16, 2002   | David J. Ecker            | To Be Assigned | 1645           | Molecular Interaction Sites of RNase P RNA and Methods of Modulating the Same       |
| 60/313,890<br>IBIS0046-001 | August 21, 2001   | David J. Ecker            | Not Applicable | Not Applicable | Molecular Interaction Sites in 16S Ribosomal RNA and Methods of Modulating the Same |
| 10/223,126<br>IBIS0046-100 | August 16, 2002   | David J. Ecker            | To Be Assigned | 1645           | Molecular Interaction Sites in 16S Ribosomal RNA and Methods of Modulating the Same |
| 09/791,147<br>IBIS0047-100 | February 22, 2001 | Richard H. Griffey et al. | J. Riley       | 1637           | Methods for Identifying Ligand Binding Sites in a Biomolecule                       |
| 10/209,692<br>IBIS0047-101 | July 31, 2002     | Richard H. Griffey et al. | To Be Assigned | 1645           | Methods for Identifying Ligand Binding Sites in a Biomolecule                       |
| 09/499,875<br>IBIS0048-100 | February 8, 2000  | Richard H. Griffey et al. | To Be Assigned | To Be Assigned | Optimization Of Ligand Affinity For RNA Targets Using Mass Spectrometry             |
| 09/573,479<br>IBIS0048-101 | May 16, 2000      | Richard H. Griffey et al. | To Be Assigned | To Be Assigned | Optimization of Ligand Affinity For RNA Targets Using Mass Spectrometry             |
| 09/630,122<br>IBIS0050-100 | August 1, 2000    | Elizabeth Jefferson       | B. Coleman     | 1624           | Antimicrobial Biaryl Compounds  |
| 08/924,851<br>IBIS0051-100 | September 5, 1997 | Eric Edward Swayze et al. | T. Prosthofel  | 1627           | Amine Compounds and Combinatorial Libraries Comprising Same                         |
| 60/291,459<br>IBIS0052-001 | May 16, 2001      | John McNeil               | Not Applicable | Not Applicable | Multi-Paradigm Knowledge-Bases  |





|   |                                   |                          |                 |      |   |
|---|-----------------------------------|--------------------------|-----------------|------|---|
| 10/150,668<br>IBIS0052-100              | May 16, 2002                      | John McNeil et al.       | To Be Assigned  | 2176 | Multi-Paradigm Knowledge-Bases  |
| 09/411,748<br>6,429,016<br>IBIS0053-100 | October 1, 1999<br>August 6, 2002 | John McNeil              | Patricia A. Bex | 1743 | System and Method for Sample Positioning in a Robotic System                        |
| 10/153,327<br>IBIS0053-101              | May 22, 2002                      | John McNeil              | To Be Assigned  | 1743 | System and Method for Sample Positioning in a Robotic System                        |
| 10/067,017<br>IBIS0054-100              | February 24, 2002                 | Michael L. Migawa        | T. McKenzie     | 1624 | Novel Pyranosyl Cytosines: Pharmaceutical Formulation and Methods                   |
| 10/071,978<br>IBIS0055-100              | February 6, 2002                  | Eric E. Swayze et al.    | K. Habte        | 1624 | Novel Benzimidazole Compounds   |
| 09/678,434<br>IBIS0056-100              | October 2, 2000                   | John McNeil              | E. Quan         | 1743 | Self-Dispensing Storage Device  |
| 09/310,844<br>IBIS0058-100              | May 12, 1999                      | David J. Ecker et al.    | M. Schmidt      | 1635 | Molecular Interaction Sites of Interleukin-2 RNA and Methods of Modulating the Same |
| 09/499,875<br>IBIS0059-100              | February 8, 2000                  | Richard Griffey et al.   | M. Tran         | 1639 | Optimization of Ligand Affinity for RNA Targets Using Mass Spectrometry             |
| 09/573,479<br>IBIS0059-101              | May 16, 2000                      | Richard Griffey et al.   | T. Prosthofe    | 1627 | Optimization of Ligand Affinity for RNA Targets Using Mass Spectrometry             |
| 10/005,344<br>ISIS0052-100              | December 4, 2001                  | Loren J. Miraglia et al. | T. Gibbs        | 1635 | Antisense Modulation of Human MDM2 Expression                                       |





|                            |                   |                       |                |      |   |
|----------------------------|-------------------|-----------------------|----------------|------|---|
| 10/281,349<br>ISIS0002-105 | October 25, 2002  | Stanley T. Crooke     | To Be Assigned | 1635 | Oligoribonucleotides and<br>Ribonucleases for Cleaving<br>RNA |
| 10/327,805<br>ISIS0060-101 | December 20, 2002 | Brett P. Monia et al. | To Be Assigned | 1635 | Antisense Modulation of<br>SMAD6 Expression                   |